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GRIGNARD REAGENTS—THEIR REDUCING ACTION AND RATES OF ADDITION

A PART OF A DISSERTATION SUBMITTED TO
THE FACULTY OF THE DIVISION OF THE
PHYSICAL SCIENCES IN CANDIDACY FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

1936

By
SIDNEY WEINHOUSE

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GRIGNARD REAGENTS—THEIR REDUCING ACTION AND RATES OF ADDITION*

SIDNEY WEINHOUSE

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INTRODUCTION

Although the reducing property of Grignard reagents first observed by Grignard¹ in 1901, has been the object of numerous subsequent investigations, relatively little progress has been made hitherto toward the formulation of a reaction mechanism, or the correlation of structure with reducing activity. In view of the widespread utilization of organomagnesium compounds in synthetic chemistry further study of this reaction appeared desirable. In the investigation reported the author had the following objectives in view: first, determination of the effect of experimental conditions (such as temperature, solvent, concentration, etc.) upon the amount of reduction observed; second, evolution of a satisfactory mechanism for the reduction process; third, establishment of a correlation, of predictive value, between the relative reducing activity of a Grignard reagent and some property of its organic radical.

Reduction by Grignard reagents is a very common phenomenon. The rôle of reduction is not always obvious, and interpretations of reactions that take an "abnormal" course often ignore it.†

* Abstracted from a dissertation submitted by S. Weinhouse to the Faculty of the Division of the Physical Sciences of The University of Chicago in August, 1935, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

¹ GRIGNARD, *Ann. chim. phys.*, [7], **24**, 468 (1901).

† Thus, the interaction of alkyl halides, such as ethyl chloride, with ethylmagnesium halides to yield ethylene and ethane may be, though seldom is, regarded as a typical Grignard reduction. In other cases, the reducing action of Grignard reagents is well recognized, as, *e.g.*, in the reduction of azobenzene and azotoluene to the respective hydrazo compounds: *cf.* FRANTZEN AND DIEBEL, *Ber.*, **38**, 2716 (1905); KIRBERG, *J. prakt. Chem.*, [2] **118**, 1, (1928). See also WIELAND AND KOGL, *Ber.*, **55**, 1798 (1922), regarding the reduction of nitroso compounds to the corresponding azo compounds. HOFFMAN, *ibid.*, **56**, 125 (1928), cites the reduction of manganous chloride to metallic manganese by means of ethylmagnesium bromide, and BUYLEA AND OLAY, *Anal. soc. españ. fis. quim.*, **20**, 599 (1922); *C. A.*, **17**, 2412

This paper is limited to a study of the reducing action of Grignard reagents on aldehydes and ketones. The authors believe, however, that the interpretation here offered can be extended to the elucidation of the reducing action of Grignard reagents in other systems.

PREVIOUS WORK

Grignard,¹ in his pioneer paper on reactions of organomagnesium compounds, reported the formation of a small amount of benzyl alcohol (in addition to 56% of 1-phenylisohexanol) when benzaldehyde was treated with isoämylmagnesium bromide. Sabatier and Maihle² noted considerable evolution of gas when cyclohexanone was treated with isopropyl- or isobutylmagnesium bromide. Later these investigators³ found that cyclohexylmagnesium chloride reduces benzophenone to benzhydrol.

The relative effectiveness of a series of alkylmagnesium bromides in the reduction of cyclohexanone and 4-methylcyclohexanone has been evaluated.⁴ The following yields of the cyclohexanols were obtained from the cyclohexanones (the respective reagents are identified by their alkyl radicals); propyl, 50%; isoämyl, 20%; isopropyl, 75%; *sec.*-octyl, 20%. Aromatic Grignard reagents had no reducing effect on the two ketones.

Konovalov, Miller, and Timtschenko⁵ have reported the formation of 38% of benzhydrol in the reaction between *tert.*-butylmagnesium bromide and benzophenone. Klages and Heilmann⁶ erroneously report the preparation of isopropyldiphenylcarbinol by the treatment of benzophenone with isopropylmagnesium bromide, since the physical constants of the product correspond with those of benzhydrol. Letellier⁷ has observed reduction when ethyl hydroxypivalate is treated with ethylmagnesium bromide. It is quite likely that the Grignard reagent first adds to the carbonyl group of the ester and that the ketone thus formed is reduced to the secondary alcohol. Gorskin⁸ records the reduction of benzopinacolone to benzopinacolyl alcohol by means of propylmagnesium iodide. Faworsky⁹ states that a 50% reduction of the aldehyde takes place in the reaction between isobutyraldehyde and *tert.*-butylmagnesium chloride.

(1922), report the formation of hydrocarbons (methane and pentane) by the reduction of sodium methylate and sodium amylate with ethylmagnesium bromide, ethylene being formed as the oxidation product.

² SABATIER AND MAIHLE, *Compt. rend.*, **138**, 1321 (1903).

³ SABATIER AND MAIHLE, *ibid.*, **139**, 345 (1904).

⁴ SABATIER AND MAIHLE, *ibid.*, **141**, 301 (1905).

⁵ KONOVALOV, MILLER, AND TIMTSCHENKO, *Chem. Zentr.*, **1906**, II, 312.

⁶ KLAGES AND HEILMANN, *Ber.*, **37**, 1451 (1904).

⁷ LETELLIER, *Compt. rend.*, **146**, 343 (1908).

⁸ GORSKIN, *J. Russ. Phys. Chem. Soc.*, **45**, 163 (1913).

⁹ FAWORSKY, *J. prakt. Chem.*, [2], **88**, 652 (1913).

Schmidlin¹⁰ obtained benzopinacol from the reaction between benzophenone and triphenylmethylmagnesium chloride. Leroide¹¹ obtained, from propylmagnesium chloride and pinacolone, a 20% yield of pinacolyl alcohol, together with propane and propylene. His data on the reducing action of several Grignard reagents on terpenic ketones and ethyl pivalate are summarized in Table I.

Hess and Wustrow¹² obtained 35–40% yields of crotonyl alcohol and cinnamic (cinnamyl) alcohol by treatment of crotonaldehyde and cinnamaldehyde, respectively, with isobutylmagnesium bromide. An ether-free coordination compound, which contained one molecule of aldehyde for each molecule of Grignard reagent, was isolated. When the coordination compound is hydrolyzed without previous heating a good yield of secondary alcohol results, but warming gives rise to evolution of isobutylene, and the residue yields only the primary alcohol. It was proved that this un-

TABLE I
REDUCTION OF TERPENIC KETONES AND ETHYL PIVALATE (LEROIDE¹¹)

CARBONYL COMPOUND	GRIGNARD REAGENT	REDUCTION (%)
Camphenylone.....	<i>n</i> -C ₃ H ₇ MgCl	100
Fenchone.....	<i>n</i> -C ₃ H ₇ MgCl	100
Camphor.....	<i>n</i> -C ₃ H ₇ MgCl	100
Ethyl pivalate.....	C ₂ H ₅ MgI	13
Ethyl pivalate.....	<i>n</i> -C ₃ H ₇ MgCl	48
Ethyl pivalate.....	<i>n</i> -C ₃ H ₇ MgBr	} Reduction; yield not stated
Ethyl pivalate.....	<i>n</i> -C ₃ H ₇ MgI	
Ethyl pivalate.....	<i>n</i> -C ₄ H ₉ MgI	

usual behavior was not due to the instability of the secondary alcohol. The same authors obtained a 60% yield of benzyl alcohol on refluxing the reaction product of benzaldehyde and ethylmagnesium bromide for some time in benzene. Without heating, however, only the normal product, 1-phenylpropanol, was obtained.

Rheinbolt and Roleff¹³ obtained a 56% yield of benzyl alcohol from the reaction between benzaldehyde and isobutylmagnesium bromide. Through a series of carefully planned experiments these investigators proved conclusively that the reductions observed do not result from decomposition of the normal addition products. Rheinbolt and Roleff¹⁴ extended their investigation to a number of other reactions and studied the effect of

¹⁰ SCHMIDLIN, *Ber.*, **39**, 4198 (1906).

¹¹ LEROIDE, *Ann. chim.*, [9], **16**, 354 (1921).

¹² HESS AND WUSTROW, *Ann.*, **437**, 256 (1924).

¹³ RHEINBOLT AND ROLEFF, *Ber.*, **57**, 1921 (1924).

¹⁴ RHEINBOLT AND ROLEFF, *J. prakt. Chem.*, [2], **109**, 175 (1925).

temperature and of order of addition upon the extent of reduction. In some cases reduction proceeds quantitatively in the cold; in other cases,

TABLE II
REDUCTION OF BENZALDEHYDE AND KETONES (RHEINBOLT AND ROLEFF¹⁴)

ORIGINAL REACTANTS	YIELDS OF REDUCTION PRODUCTS AFTER 1 HR. REFLUXING (%)	
	In ether	In benzene
Benzaldehyde + C_2H_5MgBr	11	22
Benzaldehyde + <i>cyclo</i> - $C_6H_{11}MgCl$	18	23*
Benzaldehyde + <i>i</i> - C_4H_9MgBr	55	57
Benzophenone + <i>i</i> - C_4H_9MgBr	Quantitative reduction in the cold	
Phenyl isobutyl ketone + <i>i</i> - C_4H_9MgBr	Quantitative reduction in the cold	
Benzopinacolone + <i>i</i> - C_4H_9MgBr	72	73

* In boiling anisole.

TABLE III
GRIGNARD ADDITION TO AND REDUCTION OF KETONES (STAS¹⁵)

KETONE	ALKYLMAGNESIUM BROMIDE	YIELDS (%)	
		Addition Product	Reduction Product
Diisopropyl.....	<i>i</i> - C_3H_7	0	100
Diisopropyl.....	<i>n</i> - C_3H_7	30	30
Diisopropyl.....	C_2H_5	54	21
Ethyl isopropyl.....	<i>i</i> - C_3H_7	51	30
Ethyl isopropyl.....	<i>n</i> - C_3H_7	100	0
Ethyl isopropyl.....	C_2H_5	100	0
Dipropyl.....	<i>i</i> - C_3H_7	100	0
Dipropyl.....	<i>n</i> - C_3H_7	60	20
Dipropyl.....	C_2H_5	100	0
Methyl isopropyl.....	<i>i</i> - C_3H_7	78	14
Methyl isopropyl.....	<i>n</i> - C_3H_7	100	0
Diethyl.....	<i>i</i> - C_3H_7	100	0
Diethyl.....	C_2H_5	100	0
Dimethyl (Acetone).....	<i>i</i> - C_3H_7	100	0

reduction is not complete at room temperature, but is somewhat increased at higher temperatures. Order of addition appeared to have no effect

¹⁵ STAS, *Bull. soc. chim. Belg.*, **34**, 188 (1925); **35**, 379 (1926).

on the amount of reduction in the reactions investigated. The results are summarized in Table II.

J. Stas¹⁵ found some unchanged ketone (an indication of enolization) in addition to the normal and reduction products, in the reaction between aliphatic ketones and Grignard reagents. His data are summarized in Table III. The reduction product was always accompanied by an equivalent amount of the corresponding unsaturated hydrocarbon.† Methyl- and phenylmagnesium bromides showed no reduction in any case.

Conant and co-workers¹⁶ have studied the effect of branching of the chains of alkylmagnesium halides on the yields of reduction products obtained from aldehydes, ketones, and esters, and have reached the conclu-

TABLE IV

REACTIONS OF CARBONYL COMPOUNDS WITH GRIGNARD REAGENTS (CONANT¹⁶ AND OTHER WORKERS)

CARBONYL COMPOUND	GRIGNARD REAGENT			
	CH ₃ MgI	C ₄ H ₉ MgBr	(CH ₃) ₂ CHMgBr	(CH ₃) ₃ CMgBr
CH ₃ CHO	AA	...	A	AA
(CH ₃) ₂ CHCHO	A	...	AA	AR
(CH ₃) ₃ CCHO	...	AA	AR	RR
CH ₃ COCH ₃	AA	...	AA	A
C ₂ H ₅ COC ₂ H ₅	AA	AA	AA	C
CH ₃ COCH(CH ₃) ₂	AA	...	...	...
CH ₃ COC(CH ₃) ₃	AA	AR	EC	EC
(CH ₃) ₂ CHCOCH(CH ₃) ₂	AA	...	RR	RR
(CH ₃) ₂ CHCOC(CH ₃) ₃	AA	...	RR	RR
(CH ₃) ₃ CCOC(CH ₃) ₃	AA	...	R	RR
(CH ₃) ₂ CHCO ₂ C ₂ H ₅	...	...	RR	...
(CH ₃) ₃ CCO ₂ C ₂ H ₅	...	...	...	...
C ₆ H ₅ CH ₂ CO ₂ C ₂ H ₅	...	...	EE, CC	...

sion that there is some correlation between structure and reducing activity. Conant considers that, besides the normal addition of Grignard reagents to carbonyl compounds, there are three other reactions namely, enolization, condensation of the aldol type, and reduction. The "abnormal" reactions, however, are slow, and come into play only when addition is hindered, presumably by steric effects. Table IV summarizes the observations of Conant and previous workers. The letters A, R, E, and C

† NOLLER, GREBE, AND KNOX, *J. Am. Chem. Soc.*, **54**, 4690 (1932), have proved that equivalent amounts of isobutylene and benzhydrol are formed in the reaction of isobutylmagnesium bromide with benzophenone.

¹⁶ CONANT AND BLATT, *J. Am. Chem. Soc.*, **51**, 1227 (1929); CONANT, WEBB, AND MENDUM, *ibid.*, **51**, 1246 (1929).

refer to normal addition, reduction, enolization, and condensation, respectively. Yields are not given, for the data of different investigators are not strictly comparable. However, an approximate idea of the extent of the reaction is conveyed by doubling the letters for reported yields greater than 50%.

The work of Blatt and Stone,¹⁷ however, throws some doubt upon the validity of the hypothesis that the complexity of the alkyl group and the

TABLE V
GRIGNARD ADDITION TO AND REDUCTION OF KETONES (BLATT AND STONE¹⁷)

KETONE	GRIGNARD REAGENT	ADDITION (%)	REDUCTION (%)	ENOLIZATION (%)
Dipropyl.....	<i>n</i> -C ₃ H ₇ MgBr	54	24	—
Dipropyl.....	<i>i</i> -C ₃ H ₇ MgBr	44	5	15
Propyl isopropyl.....	<i>n</i> -C ₃ H ₇ MgBr	63	17	—
Propyl isopropyl.....	<i>i</i> -C ₃ H ₇ MgBr	17	49	—
Diisopropyl.....	<i>n</i> -C ₃ H ₇ MgBr	43	34	—
Diisopropyl.....	<i>i</i> -C ₃ H ₇ MgBr	0	80	—

TABLE VI
GRIGNARD REDUCTION OF BENZOPHENONE AND RELATED KETONES (BLICKE AND POWERS¹⁸)

KETONE	GRIGNARD REAGENT	REDUCTION (%)
Benzophenone.....	CH ₃ MgI	0
Benzophenone.....	C ₂ H ₅ MgBr	0
Benzophenone.....	<i>n</i> -C ₃ H ₇ MgBr	50
Benzophenone.....	<i>i</i> -C ₃ H ₇ MgBr	22
Benzophenone.....	<i>n</i> -C ₄ H ₉ MgBr	27
Benzophenone.....	<i>i</i> -C ₄ H ₉ MgBr	74
Benzophenone.....	<i>i</i> -C ₅ H ₁₁ MgBr	30
<i>p</i> -Bromobenzophenone.....	<i>n</i> -C ₃ H ₇ MgBr	24
Phenyl naphthyl ketone.....	<i>n</i> -C ₃ H ₇ MgBr	65
Phenyl biphenyl ketone.....	<i>n</i> -C ₃ H ₇ MgBr	48
Phenyl benzyl ketone.....	<i>n</i> -C ₃ H ₇ MgBr	9

reducing activity of the reagent are directly related. Their data are summarized in Table V. Blicke and Powers¹⁸ have made a study of the reducing action of several Grignard reagents on benzophenone and related ketones (see Table VI).

Noller¹⁹ has found that isobutylmagnesium bromide, as well as diiso-

¹⁷ BLATT AND STONE, *ibid.*, **54**, 1495 (1932).

¹⁸ BLICKE AND POWERS, *ibid.*, **51**, 3378 (1929).

¹⁹ NOLLER, *ibid.*, **53**, 635 (1931).

butylmagnesium, reduces benzophenone to the extent of about 80%. Later²⁰ he extended his study to other aliphatic Grignard reagents. (See Table VII.)

Sherwood and Wallace²¹ have observed that a terpenic Grignard reagent such as bornylmagnesium chloride, reduces isovaleraldehyde to isoämyl alcohol, citral (geranial) to geraniol, and piperitone to phellandrene.

Gomberg, Bachmann, and co-workers²² have made an extensive study of the reduction of aromatic ketones to pinacols by the system Mg-MgI_2 . While this is not a strictly typical case of Grignard reduction it has been used to interpret the results of the latter reaction. The reduction of a ketone to a pinacol by the system Mg-MgI_2 is presumed to take place through the momentary formation of magnesious iodide, which may add to the carbonyl group to form a free ketyl radical in a manner analogous to the formation of ketyls by the addition of alkali metals to ketones.²³

TABLE VII
GRIGNARD REDUCTION OF BENZOPHENONE (NOLLER²⁰)

GRIGNARD REAGENT	REDUCTION (%)
<i>tert.</i> - $\text{C}_4\text{H}_9\text{MgBr}$	0
$\text{C}_2\text{H}_5\text{MgBr}$	2
<i>i</i> - $\text{C}_3\text{H}_7\text{MgBr}$	13
<i>sec.</i> - $\text{C}_4\text{H}_9\text{MgBr}$	40
<i>n</i> - $\text{C}_5\text{H}_7\text{MgBr}$	58
<i>n</i> - $\text{C}_4\text{H}_9\text{MgBr}$	59
<i>i</i> - $\text{C}_4\text{H}_9\text{MgBr}$	86

Only an infinitesimal amount of magnesious iodide is supposed to be present at any time, and in fact no weighable quantity could ever be detected; but the authors offer considerable evidence in support of the existence of this subhalide. The reduction proceeds at 0° , and is very fast at 25° (55 grams of benzophenone is reduced in five minutes to give a 99.5% yield of benzopinacol). Similar results were obtained with the system Mg-MgBr_2 , but no reduction was observed with Mg-MgCl_2 .

The work of Gomberg and Bachmann emphasizes the necessity of using filtered solutions free of metallic magnesium, and serves to explain the observations of Schmidlin,¹⁰ Lagrave,²⁴ and Arbuzov,²⁵ who obtained benzo-

²⁰ NOLLER AND HILMER, *ibid.*, **54**, 2503 (1932).

²¹ SHERWOOD AND WALLACE, *J. Chem. Soc.*, **1931**, 3340.

²² GOMBERG, BACHMANN, *et al.*, *J. Am. Chem. Soc.*, **49**, 236, 2584 (1927); **50**, 2762 (1928); **51**, 308, 2238 (1929); **52**, 2455, 3287, 3290, 4412, 4967 (1930); **53**, 1524, 2762 (1931).

²³ SCHLENK AND WEICKEL, *Ber.*, **44**, 1182 (1911).

²⁴ LAGRAVE, *Ann. chim.*, [10], **8**, 363 (1927).

²⁵ ARBUZOV AND ARBUZOVA, *J. Gen. Chem.* (U. S. S. R.), **2**, 388 (1932).

pinacol in the reaction between various Grignard reagents and benzophenone in the presence of excess magnesium. Barnett, Cook, and Nixon²⁶ and Hatt²⁷ have reduced a number of esters to the corresponding pinacols by Grignard reagents in the presence of excess magnesium, but no pinacols were obtained when the solutions were carefully filtered. Davies, Dixon, and Jones²⁸ have made identical observations regarding the reaction between benzophenone and *n*-amyl-, isoämyl-, and 1-methylbutylmagnesium bromides.

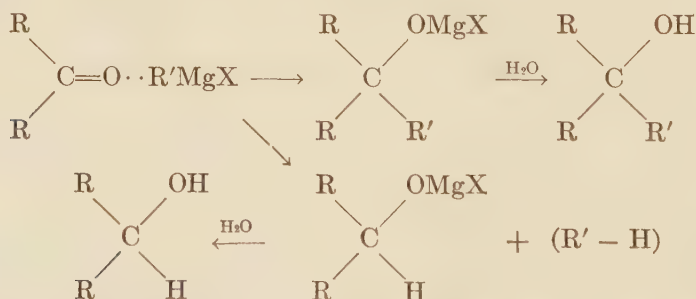
One case of similar reduction by a Grignard reagent in the absence of excess magnesium is reported by Bachmann,²⁹ who found that triphenylmethylmagnesium bromide reduces aromatic ketones to the corresponding pinacols. The reaction proceeds through the intermediate formation of free radicals, as shown by the intense coloration of the reaction mixture, and the isolation of triphenylmethyl as the oxidation product in the form of the peroxide. His results are summarized in Table VIII.

TABLE VIII
REDUCTION OF KETONES BY TRIPHENYLMETHYLMAGNESIUM BROMIDE (BACHMANN²⁹)

KETONE	REDUCTION (%)
Benzophenone.....	93
4-Chlorobenzophenone.....	78
4-Phenylbenzophenone.....	86
4,4'-Diphenylbenzophenone.....	98
Fluorenone.....	80
Xanthone.....	84

DISCUSSION

A brief discussion of some of the hypotheses which have been advanced to explain the reducing action of Grignard reagents is in order. Hess and Rheinbolt³⁰ postulate the following "mechanism":



²⁶ BARNETT, COOK, AND NIXON, *J. Chem. Soc.*, **1927**, 505.

²⁷ HATT, *ibid.*, **1927**, 898; **1929**, 1623.

²⁸ DAVIES, DIXON AND JONES, *ibid.*, **1930**, 1916.

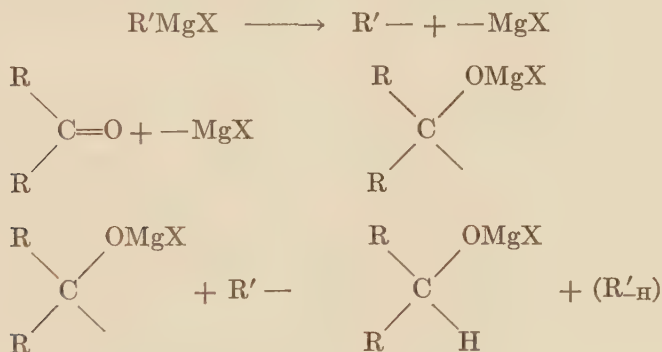
²⁹ BACHMANN, *J. Am. Chem. Soc.*, **53**, 2758 (1931).

³⁰ HESS AND RHEINBOLT, *Ber.*, **54**, 2043 (1921).

This of course is nothing more than a graphic record of the reaction. Furthermore, the formation of addition compounds is not a unique characteristic of those systems which exhibit the phenomenon of reduction, but is also observed in reactions which follow a normal course.³¹

Conant's¹⁶ postulate of the reduction process as a slow one, coming into play only when the normal addition reaction is impeded because of steric influences, is illuminating and suggestive. However, it needs further elaboration, for as is demonstrated later, many reduction reactions are extremely rapid (in some cases they are practically instantaneous), while some additions are quite slow—in fact, slower than the reduction reactions.

Blicke and Powers¹⁸ base their interpretation of the reducing action of a Grignard reagent upon the assumption that the reagent dissociates into a free organic radical and magnesium subhalide. The latter is assumed to behave like an alkali metal, and to yield, with carbonyl compounds, the corresponding ketyls. The last step in the mechanism involves intermolecular disproportionation (oxidation-reduction) of the free organic radical and the ketyl; an olefin and a secondary alcohol are thus the natural products of the reaction.



In support of this mechanism Blicke and Powers cite the observation³² that triphenylmethylmagnesium chloride is dissociated into free radicals, and furthermore that it reduces benzophenone to benzopinacol.

There are some observations, however, which are difficult to reconcile with the above mechanism of the reducing action of Grignard reagents. Thus, it would be reasonable to expect some benzopinacol when benzophenone is treated with an aliphatic Grignard reagent. Noller²⁰ records an unsuccessful search for the substance, an experience repeated by the present authors in numerous experiments. Furthermore, when a solution

³¹ MEISENHEIMER, *Ber.*, **54**, 1655 (1921); *Ann.*, **442**, 180 (1925).

³² GILMAN AND FOTHERGILL, *J. Am. Chem. Soc.*, **51**, 3149 (1929).

of bromomagnesium ketyl* was treated with an excess of butylmagnesium bromide it gave no benzhydrol; recovery of the benzopinacol was quantitative. This experiment has an important bearing upon the mechanism under discussion, for it demonstrates that the absence of benzopinacol is not due to the rapid interaction of the ketyl with the Grignard reagent to yield benzhydrol. This result raises considerable doubt as to the validity of the ketyl mechanism in reduction by Grignard reagents. Furthermore, in the absence of any experimental evidence for the dissociation of Grignard reagents into free radicals, except in organomagnesium compounds of the triarylmethyl type† there appears to be little justification for such an assumption. On the other hand, a mechanism for the reduction process based on a type of dissociation which has been adequately demonstrated experimentally, namely, dissociation into a negative organic ion and a positive halomagnesium ion, is in the author's estimation, more defensible, for it is in full accord with the experimental facts.

This mode of dissociation of the Grignard reagent may lead to a normal addition reaction, or, if other factors tend to hinder addition, the negative ion may stabilize itself in a manner characteristic of all organic oxidation-reductions namely, through the loss of a pair of electrons to the acceptor molecule. The detailed steps involved in this transfer need not concern us at this time.

This picture of the reduction process implies a relationship between the reducing activity of the Grignard reagent and the affinity of the organic radical for electrons, *i.e.*, its electronegativity.³³ From an inspection of the data collected by previous workers it can be seen that only Grignard reagents containing radicals of intermediate electronegativity cause reduction; no reduction appears to be exhibited with the strongly electronegative (aromatic) or the weakly electronegative radicals, with the exception of the very weakly electronegative triphenylmethyl radical. In the last case free-radical dissociation probably takes place, and the reduction product is, as might be expected, exclusively benzopinacol.

It is difficult, however, to draw unqualified conclusions from the available data for several reasons, most important of which is the difference in the experimental techniques employed by various investigators. Thus,

* GOMBERG AND BACHMANN, *op. cit.*, have shown that halomagnesium pinacolate, as evidenced by its intense red color, and its reduction with iodine, oxygen, etc., is dissociated to a large extent into the ketyl. The pinacolate was prepared by adding the equivalent amount of *n*-butylmagnesium bromide to a solution of benzopinacol in ether.

† Theoretically, triarylmethyl Grignard reagents, as contrasted with aliphatic and aromatic, would be expected to dissociate into free radicals.

³³ KHARASCH AND REINMUTH, *J. Chem. Educ.*, **5**, 404 (1928); **8**, 1703 (1931); KHARASCH, REINMUTH, AND MAYO, *ibid.*, **11**, 82 (1934); **13**, 7 (1936).

for the purpose of testing the hypothesis advanced, it was necessary to study the behavior of a wide variety of Grignard reagents toward a typical ketone under carefully controlled experimental conditions. Benzophenone was chosen for the following reasons: first, a considerable amount of work had already been done on this compound; second, it does not enolize; and third, the product of reduction, the halomagnesium salt of benzhydrol, is insoluble in ether. Before proceeding with this study it was necessary to determine the effect of variations in the experimental conditions upon the yield of the reduction product.

Temperature appears to exert no great influence on the yield of benzhydrol in the reaction between benzophenone and *n*-butylmagnesium bromide. Even at -80° the reaction is very fast, and a 48.5% yield of benzhydrol was obtained. At 0° and at 20° the yields of benzhydrol were 58.0 and 58.6% respectively. This is in agreement with Noller's²⁰ experiments in which a 59% yield of benzhydrol was obtained at 0 to 5° . Rheinbolt and Roleff¹⁴ have noted a slight temperature effect in the reactions between several Grignard reagents and benzaldehyde.

Order of addition likewise appeared to have little effect on the reduction. In all experiments here reported the procedure of Noller²⁰ was followed. The benzophenone, dissolved in dry benzene, was added at a uniform rate to an approximately 10% excess of a standardized solution of the Grignard reagent at such a rate that the temperature remained between 10° and 20° . When the order of addition was reversed in the reaction between *n*-butylmagnesium and benzophenone, a 63.6% yield of benzhydrol was obtained. Meisenheimer³⁴ and Marshall³⁵ have shown that reaction between aldehydes and Grignard reagents leads to reduction if an excess of the aldehyde is used, but the reduction follows a different course. The halomagnesium alcoholate, which is formed by addition of the Grignard reagent to the aldehyde, reduces the excess of aldehyde to the corresponding primary alcohol, and is simultaneously oxidized to the corresponding ketone. However, the treatment of *n*-butylmagnesium bromide with an excess (10%) of benzophenone resulted in no significant increase in reduction to benzhydrol.

The effect of solvents other than the usual benzene-ether mixture, was determined in the following way. The ether was distilled from a filtered solution of *n*-butylmagnesium bromide, and the residue was heated at 100° *in vacuo* for four hours to remove the last traces of ether. The hard, gray residual mass was broken up as well as possible, suspended in dry benzene, in which it is insoluble, and the calculated amount of benzophenone, dissolved in benzene, was added in the usual manner. A 64.5%

³⁴ MEISENHEIMER, *Ann.*, **446**, 76 (1925).

³⁵ MARSHALL, *J. Chem. Soc.*, **1925**, 2184.

yield of benzhydrol was obtained. To a similarly prepared "anhydrous" reagent pyridine was added. Considerable heat was evolved, and a yellow pyridine complex separated. Addition of solid benzophenone, in small portions, resulted in an 80% yield of benzhydrol.

In the usual procedure the concentration of Grignard reagent varied between one and two molar. In order to determine the effect of varying concentration benzophenone was added to a solution of *n*-butylmagnesium bromide of about one-tenth the usual concentration (0.141 *N*). After correction for the slight solubility of the bromomagnesium alcoholate in ether a yield of 38–45% benzhydrol was obtained.

The results in a study of benzophenone with a series of Grignard reagents ranging in the electronegativities of their radicals from phenyl to tertiary

TABLE IX
ACTION OF VARIOUS GRIGNARD REAGENTS ON BENZOPHENONE

GRIGNARD REAGENT	NORMALITY	REDUCTION (%)	ADDITION (%)
C_6H_5MgBr	1.98	0	90
$C_6H_5CH_2MgCl$	1.04	0	95
$C_6H_5CH_2MgBr$	1.54	0	52
$p\text{-}ClC_6H_4CH_2MgCl$	0.475	0	74
$tert\text{-}C_4H_9MgCl$	0.880	0	63
$CH_2:CHCH_2MgBr$	1.32	5	72
$cyclo\text{-}C_6H_{11}MgBr$	1.44	7.1	—
$C_6H_5(CH_2)_3MgBr$	1.28	20.0	38.5
$C_6H_5(CH_2)_2MgBr$	1.66	32.6	43.2
$n\text{-}C_4H_9MgBr$	1.41	58.6	—
$n\text{-}C_4H_9MgCl$	1.83	76.2	—
$i\text{-}C_4H_9MgBr$	1.86	91.0	—
$cyclo\text{-}C_6H_9MgBr$	1.86	94.0	—

butyl are shown in Table IX. The Grignard reagents were prepared in the ordinary manner, but no catalyst was used in initiating the reaction. For details of the experimental procedure see the experimental part.

These results have confirmed the previous observation that reduction occurs only with radicals of intermediate electronegativity. While, superficially, these data might seem to indicate that no correlation between the reducing action and the electronegativity of a group exists, it must be borne in mind that the normal addition reaction is proceeding simultaneously with the reduction, and therefore that the relative reaction velocities must be considered. From a theoretical standpoint it would be expected that weakly electronegative radicals, in consequence of their relatively great electron-sharing tendency, would add with relatively high velocity. Thus, while the reducing tendency is enhanced with decreasing electron

affinity, the increase in addition velocity may be even greater, proportionately, with the result in the cases of very weakly electronegative radicals, of the complete overshadowing of the reducing tendency by the relatively greater addition speed.

A search of the literature reveals only two studies of reaction rates in the addition of Grignard reagents. Gilman³⁶ and collaborators have determined the time required for complete addition of a series of Grignard reagents to azobenzene by means of the color test devised by Gilman and Schulze.³⁷ More recently Vavon³⁸ has determined the velocities of addition of several Grignard reagents to butyl benzoate. Both of these investigations point to correlation between the addition speed of a Grignard reagent and its electronegativity. Because ordinary reaction-rate studies are experimentally impossible in the reactions between Grignard reagents and ketones on account of their relatively high velocity, the author has resorted to competition experiments in which an equimolar mixture of two Grignard reagents is allowed to react with one mole of benzophenone. The hypothesis outlined leads to the conclusion that the reagent containing the less electronegative organic radical should react with the larger proportion of the ketone. The results of these experiments have confirmed the prediction.

When one equivalent of benzophenone was added to a solution containing one equivalent each of *n*-butylmagnesium bromide and benzylmagnesium chloride no reduction occurred and a 65% yield of benzyldiphenylcarbinol was obtained. No benzhydrol was isolated in spite of the fact that the experimental method is capable of detecting as little as a few per cent. In a similar experiment with *n*-butylmagnesium bromide and phenylmagnesium bromide reduction occurred to the extent of 43%, and no triphenylcarbinol could be isolated. With an equimolar mixture of phenylmagnesium bromide and benzylmagnesium chloride, benzyldiphenylcarbinol was obtained in greater than 75% yield, but no triphenylcarbinol could be detected. Whereas isobutylmagnesium bromide itself reduces benzophenone to the extent of 91%, a mixture of the former with *tert*.-butylmagnesium chloride yielded only *tert*.-butyldiphenylcarbinol, and no reduction was observed. In another experiment, after the addition of benzophenone to a mixture of phenylmagnesium bromide and *tert*.-butylmagnesium chloride, carbon dioxide was passed into the solution. A yield of 91% of benzoic acid, calculated on the basis of the phenylmagnesium bromide used, was obtained. This indicates that little, if any, of the phenyl Grignard reagent added to the benzophenone in the presence

³⁶ GILMAN, HECK, AND ST. JOHN, *Rec. trav. chim.*, **49**, 212 (1930).

³⁷ GILMAN AND SCHULZE, *J. Am. Chem. Soc.*, **47**, 2002 (1925).

³⁸ VAVON, BARBIER, AND THIEBAUT, *Bull. soc. chim.*, [5], **1**, 806 (1934).

of *tert.*-butylmagnesium chloride. Finally, benzophenone was treated with a mixture of phenylmagnesium bromide and a Grignard reagent of a more electronegative radical, namely, α -naphthylmagnesium bromide. In this experiment, a 76% yield of triphenylcarbinol was obtained, and steam-distillation of the reaction mixture after hydrolysis yielded 71% of naphthalene.

These competition experiments clearly indicate a definite relationship between the electronegativity of a group and its speed of addition in the Grignard reaction. Indeed the apparent one-sidedness of these reactions is all the more striking, since the more reactive of the two reagents is constantly being used up through addition to the ketone, thus leaving a pre-

TABLE X
CORRELATION BETWEEN ELECTRONEGATIVITY AND REDUCING ACTIVITY OF
GRIGNARD RADICALS
(Alkylmagnesium Halides + Benzophenone)

RADICAL	REDUCTION (%)
C_2H_5-	2
$n-C_3H_7-$	58
$n-C_4H_9-$	59
$i-C_4H_9-$	91
$cyclo-C_5H_9-$	94
$sec.-C_4H_9-$	40
$i-C_8H_{11}-$	30
$C_6H_5(CH_2)_2-$	33
$C_6H_5(CH_2)_3-$	20
$cyclo-C_6H_{11}-$	7
$CH_2:CHCH_2-$	ca. 5

ponderance of the less reactive reagent in solution. If the radicals studied in these orientation experiments are arranged in the order of their addition velocities the following series is obtained: *tert.*-butyl > benzyl > isobutyl > *n*-butyl > phenyl > α -naphthyl. This order is without exception the same as the order obtained when the radicals are arranged according to increasing electronegativity. The striking agreement between the two properties could hardly be considered a result of pure chance.

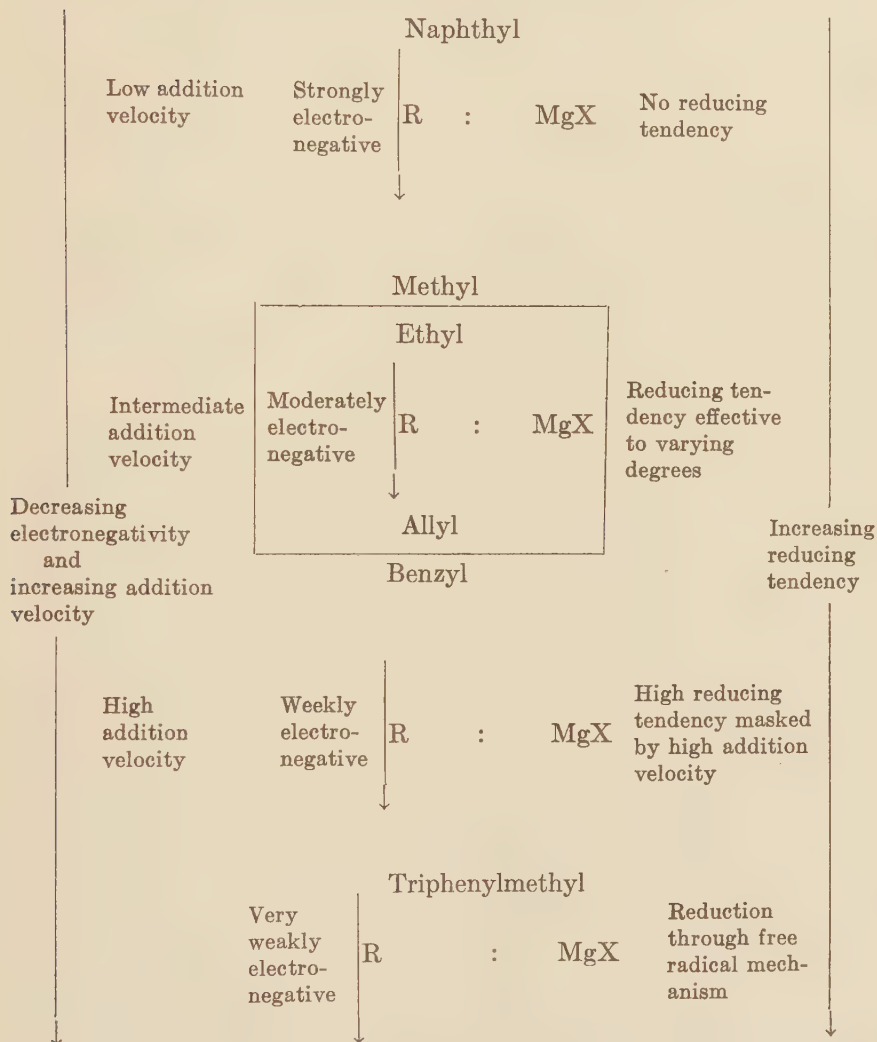
With the results of these orientation experiments in mind, the reader will see more clearly in Table X the interesting relationship between the relative electronegativity of a group and its reducing tendency.

It will be noticed upon inspection of the table that as the electronegativity is decreased, the percentage of reduction increases to a certain point and then progressively falls off. This behavior is ascribed, not to a reduc-

ing tendency which increases and then decreases, but to a constantly increasing reducing tendency, on which is superimposed a more rapidly increasing addition velocity.

FIGURE 1

SCHEMATIC CORRELATION OF RADICAL ELECTRONEGATIVITIES WITH ADDITION-REDUCTION TENDENCIES OF GRIGNARD REAGENTS AS EXHIBITED TOWARD BENZOPHENONE



As a basis for predicting the behavior of a particular Grignard reagent, we may establish four classifications:

One: Those reagents containing strongly electronegative radicals, for which the addition velocity is small, but in which the reducing tendency is absent.

Two: Those reagents containing radicals of intermediate electronegativity, which add and reduce in varying proportions.

Three: Those reagents containing weakly electronegative radicals with strong reducing tendencies, which are, however, completely masked by very great addition velocities.

Four: Those reagents containing very weakly electronegative radicals which exhibit the phenomenon of free-radical dissociation and give rise to a somewhat different type of reduction (Fig. 1).

Only radicals which fall into groups two and four will cause reduction. If the triarylmethyl Grignard reagents are excluded it may be said that that reagents containing radicals either more electronegative than ethyl, or less electronegative than allyl, will not exhibit this property. Although this study has been restricted to only one ketone, the foregoing literature survey indicates that the above predictive generalizations would hold in the reactions of Grignard reagents with other ketones, except for the possibility of minor shifts in the dividing lines between the various groups.

EXPERIMENTAL PART

The Grignard reagents were prepared in a special three-necked flask, into the bottom of which was sealed a sintered glass disc and a vertical tube which could be closed by means of a stopcock. The design of the flask allowed easy, quick filtration of the reagent by means of dry nitrogen pressure through the sintered glass filter.

The anhydrous ether was prepared by washing the commercial product with dilute potassium permanganate solution until there was no further decolorization; then with water. The ether was dried successively with calcium chloride and sodium, and distilled from the sodium into a dark stock bottle, in which it was kept over sodium wire. Unless otherwise indicated, the chemicals used were obtained from the Eastman Kodak Co., and purified by distillation or crystallization immediately before using.

Approximately six moles of ether was used for each mole of halide, and the following procedure was adopted. One-third the required quantity of ether was poured into the flask onto about a 10% excess of magnesium turnings (commercial variety), the rest of the ether being used to dissolve the halide. A few cubic centimeters of the halide solution was added dropwise from a dropping funnel, and when the reaction was slow in starting the solution was warmed gently with a micro burner. When reaction began the remainder of the halide, dissolved in ether, was added at such a rate that the ether was kept gently refluxing without external application of heat.

After addition of the halide was completed, the solution was refluxed with continued stirring for a half-hour, and then allowed to cool. The Grignard reagent was filtered through the sintered glass disc by means of dry nitrogen pressure into a graduated Erlenmeyer flask and a 2-cc. aliquot was removed for titration. The flask was then fitted with a thermometer and dropping funnel. The required amount of benzophenone, dissolved in approximately twice its weight of dry benzene, was

placed in the dropping funnel and the flask was cooled in ice. When the temperature reached 10° the ketone was added dropwise at such a rate that the temperature remained between 10 and 20°. During addition the contents of the flask were stirred by swirling the flask vigorously.

Addition of benzopinacol to n-butylmagnesium bromide.—To 100 cc. of a 1.77 *N* solution of *n*-butylmagnesium bromide was added 16.0 g. (.044 mole) of benzopinacol with stirring. The deep violet color of the "ketyl" appeared, and part of the salt separated, but redissolved on the addition of 25 cc. of benzene. After the clear violet solution had stood for four hours it was hydrolyzed by pouring into dilute hydrochloric acid, and the mixture was extracted four times with 25-cc. portions of ether. The colorless residue left after evaporation of the solvent was extracted twice with 10-cc. portions of cold alcohol to remove any benzhydrol. The residue, melting at 175–178°, weighed 13.3 g. Evaporation of the alcohol extract yielded 0.1 g. of residue melting at 168°. No benzhydrol was isolated.

Effect of temperature in the addition of benzophenone to n-butylmagnesium bromide.—A 1.77 *N* solution of *n*-butylmagnesium bromide was divided into three 100-cc. portions which were treated in the following ways.

(1) Eighteen grams of benzophenone was added in the usual manner while the temperature was kept between 10 and 20°. Immediately upon addition of the ketone a violet-red color appeared, and before addition was complete, the insoluble bromomagnesium alcoholate began to precipitate. When addition was complete, the mixture was allowed to stand for about a half-hour at room temperature, and then filtered quickly through a 7.5-cm. Buchner funnel. The precipitate was washed with three 10-cc. portions of anhydrous benzene, then transferred quickly back to the flask and hydrolyzed with dilute hydrochloric acid. The hydrolysate was then extracted three times with ether, and the combined ether extracts were evaporated to dryness on the steam bath. The solid residue was dried in a vacuum desiccator. Yield of benzhydrol (m.p. 64–65°), 10.6 g., 58.6%.

(2) The procedure followed was exactly the same as for (1), except that the temperature during addition was kept between –5° and 0° by means of an ice-salt mixture. Yield of benzhydrol (m.p. 63–65°), 10.5 g., 58.0%.

(3) The procedure was the same as for (1) and (2) except that the temperature was kept at –80° with solid carbon dioxide. In this case, the mixture was not allowed to warm up to room temperature, but was filtered immediately after addition. Yield of benzhydrol (m.p. 64–65°), 8.8 g., 48.5%.

Effect of reversal of addition.—A 100-cc. portion of a 1.77 *N* solution of *n*-butylmagnesium bromide was filtered directly into a dropping funnel and added in the usual manner to a solution of 18.0 g. of benzophenone in 40 cc. of dry benzene. Working up of the precipitate in the above-described manner yielded 11.5 g. (63.6%) of benzhydrol (m.p. 62–64°).

Effect of excess benzophenone.—To 50 cc. of a 1.41 *N* solution of *n*-butylmagnesium bromide was added 14.3 g. (0.079 mole) of benzophenone in 30 cc. dry benzene. Working up in the usual way, 9.3 g. of benzhydrol (m.p. 62–64°) was obtained. Yield, 64.3%.

Effect of concentration of the Grignard reagent.—Ten cubic centimeters of a 1.41 *N* solution of *n*-butylmagnesium bromide was diluted to 100 cc. and 2.1 g. of benzophenone dissolved in 5 cc. of benzene was added in the usual way. A total of 0.8 g. of benzhydrol (m.p. 63–65°) was isolated. After correction for the slight solubility of the bromomagnesium salt of benzhydrol in ether, the yield was estimated to be between 38 and 45%.

Addition of benzophenone to n-butylmagnesium bromide in benzene.—After several unsuccessful attempts to prepare the Grignard reagent in benzene, the following

method was finally adopted to obtain an ether-free Grignard reagent. A 1.70 *N* solution of *n*-butylmagnesium bromide in ether (75 cc.) was transferred to a 200-cc. round-bottomed flask, and the ether was evaporated under reduced pressure. The last traces of ether were then removed by heating the flask for four hours at 100° *in vacuo*. The gray amorphous residue showed some tendency to sublime during heating. The flask was then cooled, 75 cc. of anhydrous benzene was added, and the hard mass was broken up as well as possible with a stirring rod. While the flask was cooled in ice, 15.0 g. of benzophenone, dissolved in 30 cc. of dry benzene, was added at a slow, regular rate. The usual red color appeared and a heavy, white precipitate formed. The mixture was allowed to stand one hour, then filtered, and the residue was hydrolyzed with dilute acid. After extraction with ether and working up of the extract as usual, 9.80 g. of benzhydrol (m.p. 64–65°) was obtained. Yield, 64.5%.

Addition of benzophenone to n-butylmagnesium bromide in pyridine.—To a similarly prepared "anhydrous" reagent was added 75 cc. of dry pyridine. A great deal of heat was liberated in this process and considerable care was required to prevent the reagent from becoming too hot. This was accomplished by adding the pyridine slowly in small portions with continuous cooling and stirring. The solution took on a deep yellow color and a lemon-yellow pyridine complex separated. To this well-stirred suspension was added 15.0 g. of benzophenone in small portions, while ice-bath cooling was continued. A momentary green coloration developed on the addition of each portion of benzophenone. After about an hour's standing the mixture was hydrolyzed with dilute sulfuric acid, enough acid being added to give a red color when tested with methyl orange. Extraction with ether and evaporation of the solvent yielded 12.2 g. (80.0%) of benzhydrol (m.p. 64–65°).

Addition of benzophenone to benzylmagnesium chloride.—Benzophenone (45.5 g.) was added to 300 cc. of a 1.04 *N* solution of benzylmagnesium chloride. A momentary violet coloration developed after each addition of benzophenone, but after completion of addition no precipitate had formed and the solution was a faint green in color. After standing a half-hour, the solution was hydrolyzed, extracted with ether, and the ether was evaporated. The residue was crystallized from 95% alcohol. The first crop yielded 57 g. of colorless crystals; m.p. 87.5–88.5°. Upon working up the mother liquor an additional lot of 6.1 g. (m.p. 85–87°) was isolated. Total yield of benzyldiphenylcarbinol, 95%.

Addition of benzophenone to benzylmagnesium bromide.—The procedure followed was the same as for the chloride. No precipitate of the bromomagnesium benzhydrylate appeared, and a 52% yield of benzyldiphenylcarbinol was obtained; m.p. 85–87°.

Addition of benzophenone to p-chlorobenzylmagnesium chloride.—Benzophenone (7.0 g.) in 15 cc. of dry benzene was added to .038 moles of a 0.475 *M* solution of *p*-chlorobenzylmagnesium chloride. The usual momentary red color was exhibited and a white precipitate formed. This was filtered and worked up as usual. The solid product obtained was recrystallized from hot 95% alcohol. Yield 8.8 g.; m.p. 116.5–117.5°. One recrystallization from alcohol raised the melting point to 117.5–118.5°, at which point it remained constant upon further recrystallization.

Analysis for Cl: Found, 11.25%, Calc'd for *p*-chlorobenzyldiphenylcarbinol, 11.49%.

Addition of benzophenone to tert.-butylmagnesium chloride.—Because of the abnormally low yield of Grignard reagent obtainable by the use of *tert.*-butyl bromide (about 25%), the chloride was used. Average yields of 60% were obtained with this reagent. To 185 cc. of a 0.880 *N* solution of *tert.*-butylmagnesium chloride 30 g.

of benzophenone was added in the usual manner. The usual red coloration appeared, but no precipitate formed. After a half-hour's standing the clear solution was hydrolyzed and worked up in the usual way. The product obtained was a viscous yellow oil, which distilled at 160–162° under a pressure of 5 mm. After a second distillation 23.8 g. of a colorless oil having a refractive index of 1.5722 was obtained. (*tert.*-Butyldiphenylcarbinol: b.p. 178–180°/11 mm.; n_D^{15} 1.5731.)³⁹ Yield, 63%.

Addition of benzophenone to allylmagnesium bromide.—Benzophenone (18.2 g.) was added in the usual way to 100 cc. of a 1.32 *N* solution of allylmagnesium bromide. No precipitate formed. The red solution was hydrolyzed, and after working up, the oily product was distilled under reduced pressure. Yield of allyldiphenylcarbinol (b.p. 150–155°/3 mm.), 72%. A small amount of yellow, gummy matter remained in the flask after distillation. This was washed out with acetone, and the acetone was evaporated. The gum was taken up in hot alcohol and on cooling 0.6 g. of white crystals was obtained; m.p. 105–106°. Recrystallization from alcohol raised the melting point to 107–109°. This substance was shown by means of a mixture melting-point determination to be dibenzhydryl ether;⁴⁰ m.p. 108–109°.

Oxidation of allyldiphenylcarbinol.—A sample (2.2 g.) of the product obtained in the above reaction was refluxed with 4.2 g. of potassium permanganate in 80 cc. of water until the color of the permanganate was discharged. The solution was filtered from manganese dioxide and the filtrate was extracted with ether. Acidification of the aqueous portion yielded a flocculent white precipitate which was filtered, washed with water, and dried; m.p. 208–209°. (Melting point of β -hydroxy- $\beta\beta$ -diphenylpropionic acid, 212°.)⁴¹

Addition of benzophenone to cyclohexylmagnesium bromide.—Benzophenone (21.0 g.) dissolved in 40 cc. of anhydrous benzene was added to 110 cc. of a 1.44 *N* solution of cyclohexylmagnesium bromide in the usual manner. The usual red coloration appeared, and near the end of the addition a small amount of precipitate formed. After a half-hour's standing the solution was filtered, and the precipitate and the filtrate were hydrolyzed and worked up separately. The precipitate yielded 1.70 g. (7.1%) of benzhydryl (m.p. 59–61°). The filtrate yielded a colorless oil with a pronounced camphor-like odor. On distillation under reduced pressure a considerable quantity of water was given off and 21.5 g. of distillate was collected, over a range of 150 to 220° at 8 mm. All attempts to crystallize this product were unsuccessful.

Preparation of γ -phenylpropyl bromide.—Cinnamic (cinnamyl) alcohol (134 g.) was treated with hydrogen under a pressure of three atmospheres in the presence of a Raney nickel catalyst. Absorption of hydrogen was very rapid. The reduction was continued until hydrogen absorption ceased (about four and a half hours). The product was then distilled under reduced pressure, the fraction boiling at 124–125°/15 mm. being collected. Yield, 118 g., 87%.

A 68-g. lot of the hydrocinnamic alcohol so obtained was refluxed for two hours with 170 g. (2 moles) of a 48% aqueous solution of hydrogen bromide. After cooling, the two layers were separated; the bromide layer was washed with concentrated hydrochloric acid, then with cold water, and finally was dried with anhydrous sodium sulfate. The product was then fractionated under reduced pressure; b.p. 108–109°/11 mm.; yield, 69.6 g. (70%).

Addition of benzophenone to γ -phenylpropylmagnesium bromide.—To 100 cc. of a

³⁹ RAMART-LUCAS, *Compt. rend.*, **154**, 1088 (1912).

⁴⁰ KNOEVENAGEL AND HECKEL, *Ber.*, **36**, 2827 (1903).

⁴¹ RUPE AND BUSOLT, *ibid.*, **40**, 4538 (1907).

1.28 *N* solution of γ -phenylpropylmagnesium bromide (obtained in 86% yield) was added 18.0 g. of benzophenone. The precipitate was filtered, and the precipitate and filtrate were hydrolyzed separately. The precipitate yielded 3.60 g. (20.0%) of benzhydrol; m.p. 59–61°. The filtrate yielded 11.5 g. of a crystalline product melting at 68–72°. Recrystallization from alcohol, and then from ligroin, raised the melting point to 74–75°. Yield of γ -phenylpropyldiphenylcarbinol, 38.5%.

Dehydration of γ -phenylpropyldiphenylcarbinol.—A 1.0 g. lot of the product was dissolved in 50 cc. of dry benzene, and an excess of phosphoric anhydride was added. The mixture was heated to its boiling point on the water bath for 30 minutes and then allowed to cool. The solution was then filtered from the P_2O_5 and the benzene was evaporated. The colorless dehydration product melted at 122–123° (1,1,4-Triphenylbutene-1, m.p. 122–124°).⁴²

Preparation of phenethyl (β -phenylethyl) bromide.—Phenethyl (β -phenylethyl) alcohol (75 g.) was refluxed for two hours with 285 cc. of 48% hydrobromic acid (mol. ratio, 1:4). After cooling, the upper bromide layer was washed with cold water, dried with anhydrous sodium sulfate, and fractionated; b.p. 109–110°/24 mm. Yield, 86 g. (76%).

Addition of benzophenone to phenethylmagnesium bromide.—Addition of 25 g. of benzophenone to 110 cc. of a 1.66 *N* solution of phenethylmagnesium bromide (obtained in 92% yield) resulted in the isolation of 8.2 g. of benzhydrol (m.p. 58–61°); yield 32.6%.

Hydrolysis of the filtrate yielded 14.5 g. of a solid crystalline product, which after recrystallization from alcohol melted at 85–86°. (Phenethyldiphenylcarbinol, m.p. 85–87°).⁴³

*Addition of benzophenone to *n*-butylmagnesium chloride.*—A 25 g. lot of benzophenone in 40 cc. of dry benzene was added to 80 cc. of a 1.46 *N* solution of *n*-butylmagnesium chloride. The usual red coloration appeared, and precipitation began immediately. Recovery in the usual way yielded 20.6 g. of benzhydrol (m.p. 62–64°); 76%.

Addition of benzophenone to isobutylmagnesium bromide.—Benzophenone (13.0 g. in 20 cc. dry benzene) was added to 36 cc. of a 1.86 *N* solution of isobutylmagnesium bromide. The precipitate yielded 12.0 g. (91%) of benzhydrol; m.p. 62–64°.

Addition of benzophenone to cyclopentylmagnesium bromide.—The cyclopentylmagnesium bromide was prepared by the usual Grignard procedure, which resulted in a 93.5% yield of the reagent. The cyclopentyl bromide was prepared by the following series of reactions, according to the method of Adams:⁴⁴ cyclohexanol $\rightarrow$ adipic acid $\rightarrow$ cyclopentanone $\rightarrow$ cyclopentanol $\rightarrow$ cyclopentyl bromide. To 100 cc. of a 1.86 *N* solution of the reagent was added 25 g. of benzophenone in 40 cc. of dry benzene. The usual procedure for working up the reduction product yielded 23.5 g. (91%) of benzhydrol; m.p. 61–63°.

*Addition of benzophenone to a mixture of *n*-butylmagnesium bromide and benzylmagnesium chloride.*—A solution containing 0.084 mole of each of the two Grignard reagents was made up to 100 cc. with ether, and 14.0 g. of benzophenone (0.077 mole) in 30 cc. of dry benzene was added at a slow, uniform rate. Although the usual red coloration appeared, no precipitate formed. After standing a half-hour, the solution was hydrolyzed, extracted with ether, and the ether was evaporated. The

⁴² WOOSTER AND RYAN, *J. Am. Chem. Soc.*, **54**, 2419 (1932).

⁴³ PATERNO AND CHIEFFI, *Gazz. chim. ital.*, **39**, II, 423 (1909).

⁴⁴ ADAMS AND NOLLER, *J. Am. Chem. Soc.*, **48**, 1080 (1926).

crystalline residue was recrystallized from 95% alcohol, yielding 11.9 g. of a colorless product melting at 82–84°. Recrystallization from ligroin raised the melting point to 87–88°. Yield of benzyldiphenylcarbinol, 56%. No benzhydrol could be isolated.

Addition of benzophenone to a mixture of phenyl- and n-butylmagnesium bromides.—To 100 cc. of a solution containing 0.084 mole of each of the two Grignard reagents was added 14.0 g. of benzophenone in 30 cc. dry benzene. After standing one-half hour, the solution was filtered, and the precipitate and filtrate were hydrolyzed and worked up separately. The precipitate yielded 4.6 g. (33%) of benzhydrol (m.p. 61–64°). No triphenylcarbinol could be isolated from the hydrolysis products of the filtrate.

Addition of benzophenone to a mixture of phenylmagnesium bromide and benzylmagnesium chloride.—A 14.0 g. lot of benzophenone in 30 cc. dry benzene was added to 100 cc. of a solution containing .084 mole of each Grignard reagent. After exhaustive fractional crystallization of the reaction product, 16.7 g. (a 79% yield) of benzyldiphenylcarbinol (m.p. 88.0–88.5°) was obtained. No triphenylcarbinol could be isolated.

Addition of benzophenone to a mixture of isobutylmagnesium bromide and tert.-butylmagnesium chloride.—Thirteen grams (.072 mole) of benzophenone in 25 cc. of benzene was added to 100 cc. of a solution containing .080 mole of each of the two Grignard reagents. The usual red coloration appeared during addition, but no precipitate formed, indicating that no reduction had occurred.

Addition of benzophenone to a mixture of phenylmagnesium bromide and tert.-butylmagnesium chloride.—Eleven grams of benzophenone in 20 cc. of dry benzene was added to 100 cc. of a mixture containing .069 mole of each Grignard reagent. After completion of addition the clear red solution was carbonated with powdered solid carbon dioxide. After standing one hour the solution was hydrolyzed with dilute hydrochloric acid, and extracted with four portions of ether. The ether extract was then shaken with three 25-cc. portions of dilute sodium hydroxide solution, and the aqueous extract was acidified by the addition of dilute hydrochloric acid. The white precipitate was filtered and dried; m.p. 118–120°; weight 6.0 g. Concentration of the mother liquor yielded another crop of crystals weighing 1.9 g.—a total of 7.9 gms. of benzoic acid, corresponding to a yield of 94%.

Addition of benzophenone to a mixture of phenyl- and α -naphthylmagnesium bromides.—Benzophenone (16.4 g. in 30 cc. of dry benzene) was added to 110 cc. of a mixture containing 0.100 mole of each Grignard reagent. The semi-solid residue obtained by the usual method of recovery was steam-distilled. After cooling, the solid residue from the steam-distillation was extracted and the extract was allowed to crystallize from a mixture of benzene and ligroin; 13.3 g. of triphenylcarbinol, (m.p. 159–160°) was obtained. Fractional crystallization of the mother liquor yielded an additional 4.5 g. of triphenylcarbinol—a total yield of 76%. Further fractionation of the mother liquor yielded 0.7 g. of α -naphthylidiphenylcarbinol (m.p. 135–136°). From the distillate, 9.1 g. (a yield of 71%) of naphthalene was obtained.

SUMMARY

1. The literature pertaining to the reducing action of Grignard reagents has been reviewed.

2. A study of the behavior of a series of Grignard reagents containing

radicals of a considerable electronegativity range (from α -naphthyl to *tert.*-butyl) reveals that reduction is caused only by radicals of intermediate electronegativity.

3. The effect of experimental conditions upon the reducing action of Grignard reagents has been evaluated.

4. A study of the velocities of addition of a series of Grignard reagents to benzophenone shows that rate of addition increases with decreasing electronegativity of the radical.

